Protein in Critically ill: Maintenance of Muscle Mass and Performance

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Disclosure of potential conflicts of interest during the last 2 years:

Member of the Medical Advisory Boards and also invited speaker for Baxter, Danone, Fresenius-Kabi, GE Health Care, Grifols, and Nestlé
Protein in Critical Illness: Muscle mass and performance

1. Muscle mass
2. Nitrogen balance
3. Observational studies
4. Randomized studies
5. Protein turnover
Reid et al, Clin Nutr 2004;23:273-80
15%/week
Figure 5. Measurements of Muscle Wasting During Critical Illness by Organ Failure

Data are expressed as medians and 95% confidence intervals.

\( a \) P<.03 for change from day 1 to day 3 in multiorgan failure vs single organ failure.
\( b \) P<.001 for change from day 1 to day 7 and day 1 to day 10 in multiorgan failure vs single organ failure.

\( c \) P<.001 for difference between failure of 2-3 organs and 4-6 organs from day 1 to day 7 and day 10.

Puthucheary et al. JAMA 2013
Figure 1. Representative patient showing transverse computed tomography image at the 3rd lumbar vertebrae demonstrating subcutaneous adipose tissue (light blue), abdominal skeletal muscle (red), intermuscular fat (green) and visceral fat (yellow).
Distance walked in 6 minutes

Herridge et al. NEJM 2003
Protein in Critical Illness

Muscle Mass

There is a muscle protein depletion of 10% per week initially in critical illness.

Muscle mass is a predictor for ICU survival.

Regain of muscle mass and function is slow.
Dickerson et al, J Trauma Acute Care Surg 2012;73:549-557
Dickerson et al, J Trauma Acute Care Surg 2012;73:549-557
Larsson et al, Br J Surg 1990;77:413
Larsson et al, Br J Surg, 1990;77:413-6
Protein in Critical Illness

Nitrogen balance

For reliable results there must be an adapted steady state in both caloric and protein intake.

Furthermore the study subjects must be in a steady state during that adaptive period.

Ergo. Nitrogen balance has considerable limitations in critical illness
Change in Total Body Protein

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Protein (g/kg/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (n = 7)</td>
<td>1.14 ± 0.13(^a,b)</td>
</tr>
<tr>
<td>B (n = 8)</td>
<td>1.47 ± 0.11(^b)</td>
</tr>
<tr>
<td>C (n = 8)</td>
<td>1.86 ± 0.14(^b)</td>
</tr>
</tbody>
</table>

Ishibashi et al, CCM 1998;26:1529-35
Allingstrup et al,
Clin Nutr 2012;31:462-8
Weijs et al, 
Crit Care 2014;18:701
Zusman et al, Crit Care 2016;20:367
Protein in Critical illness

Observational studies

Even when prospective in character, observational studies are case series where the variation in protein intake usually relates to the fixed proportions between calories protein in commercial products and the success in the feeding protocol.

Ergo. Hypothesis generating and possibly good for safety evaluation, but do not allow for conclusions of treatment.
Allingstrup et al, ICM 2017;43:1637-47
Allingstrup et al, ICM 2017;43:1637-47
Doig et al, ICM 2015;41:1197-1208
controls (n=235)
protein (n=239)

mortality rate (%)

<table>
<thead>
<tr>
<th></th>
<th>ICU</th>
<th>hospital</th>
<th>90 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>controls</td>
<td></td>
<td>P = 0.78</td>
<td></td>
</tr>
<tr>
<td>protein</td>
<td>10</td>
<td>P = 0.46</td>
<td>P = 0.56</td>
</tr>
</tbody>
</table>

Doig et al, ICM 2015;41:1197-1208
Protein in Critical illness

Prospective studies

Existing prospective randomized studies are few and have limitations in design.

Nevertheless there is no evidence so far to support the hypothesis of beneficial effects with a higher protein intake.
Whole body protein turnover

-40
-30
-20
-10
0
10
20
30
40
control control fed septic Fed

Leu mg/kg/h

Breakdown
Balance
Synthesis

Rooyackers et al. Clin Nutr 2015;34:95-100
Berg et al. Critical Care 2013;17:R158
B

Phenylalanine oxidation (μmol/kg/h)

Amino acids/protein feeding (g/kg/day)

Liebau et al. Critical Care 2015 19:844
1.11 g/kg (0.59-1.72) 1.74 g/kg (0.56-2.68)

Sundström Rehal et al. Critical Care 2017 21:298
Protein in Critical Illness

Whole body protein turnover

Singular measurements are snapshots. Enteral intake is difficult to monitor. Isotopic labelling of different amino acids gives slightly different results.

The litterature is so far limited.

Ergo. Can potentially become gold standard to evaluate protein needs.
Catabolism

Proteolysis

Synthesis
Tjäder et al, Clin Nutr 2005
Gamrin-Gripenberg et al. Crit Care 22:13, 2018
Gamrin-Gripenberg et al. Crit Care 22:13, 2018
Protein in Critical Illness

Muscle protein turnover

Differences in muscle protein content are difficult to measure with sufficient precision.

Differences in muscle protein synthesis and degradation are possible to measure, but reliable technique is invasive.

For ICU longstay muscle protein depletion levels out.
In conclusion

Despite more than 50 years of practice in clinical nutrition, protein needs for the critically ill is still not known.

Techniques to assess whole body protein metabolism and muscle protein metabolism are at hand, but with inherent limitations.
Our research is dedicated to the metabolic and nutritional problems of critically ill patients treated in the ICU.

We are a small research group dedicated to the metabolic and nutritional problems of critically ill patients in the intensive care unit (ICU).
Thank you for listening